Abstract

The present invention is a process for the preparation of 17β-hydroxy-7α-methyl-19-nor-17α-pregn-5(10)-en-20-yn-3-one (17α-ethynyl-17β-hydroxy-7α-methyl-5(10)-estren-3-one, tibolone) of formula 1, which comprises hydrolysis of 17α-ethynyl-17β-hydroxy-7α-methyl-5(10)-estrene 3,3-cyclic ketals of formula 2, where groups R_1, R_2, R_3 and R_4 are hydrogen atoms or alkyl groups, or R_1 and R_3, taken together with the carbon atoms within the dioxolane ring to which they are attached, form an alicyclic ring fused to the dioxolane ring, with R_2 and R_4 being hydrogen atoms, or R_1 and R_3 together with the carbon atoms to which they are attached form an aromatic ring fused to the dioxolane ring, where R_2 and R_4, taken together, form a chemical bond within said aromatic ring.

In addition, the present invention includes an intermediate, compound of formula 2 and two processes to prepare 17α-ethynyl-17β-hydroxy-7α-methyl-5(10)-estrene 3,3-cyclic ketals of formula 2: (a) by contacting 17α-ethynyl-17β-hydroxy-7α-methyl-4-estren-3-one with vicinal diols in the presence of a protic acid, and (b) by contacting 7α-methyl-5(10)-estrene-17-one 3,3-cyclic ketals of formula 4, where R_1-R_4 are defined as above, with metal acetylides, in inert solvents.

23 claims